

# Investigation into Amino Acid Racemization Pathways using Computational Chemical Methods

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Apart from glycine, all amino acids exist in two or more thermodynamically equivalent stereochemical isomers (D- and L-isomers). Biogenesis of proteins almost exclusively generates polymers with an L-configuration. With increasing age or temperature L-amino acids undergo racemization to their corresponding D-isomers, eventually resulting in a D/L ratio of 1 for fully racemized amino acid mixtures. Because of this, a measurement of the D/L ratio of samples could potentially be used to determine either age or thermal history. However, as a dating tool, racemization has proved controversial (Pollard & Heron, 1996). One potential reason for these failures in amino acid racemization chronology may lie in the complexity of the chemical reactions involved. At this moment, three distinctly different racemization pathways are known to occur, (1) direct isomerisation by formation of carbanions, (2) dipeptide condensation at the N-terminal of the polypeptide (DKP-formation, Gaines & Bada, 1988) and (3) deamidation of specific amino acid residues (aspartic acid and asparagine) to form succinimide intermediates (Geiger and Clarke, 1987). Parameters like physical and chemical environment (temperature, pH) and polypeptide sequence and conformation (van Duin and Collins, 1998) are likely to affect each of these isomerisation pathways

differently. To determine how each of these three racemization pathways affects the individual amino acid monomers we have been performing a range of computational chemical simulations. In these simulations the stabilities of the amino acid carbanions were determined using quantumchemical methods. In cases where the carbanion stabilities failed to explain observed racemization rates additional simulations were performed to determine whether any of the two other mechanisms could be responsible for these deviations. The results from these simulations allow us to sketch a more complete picture of the complex chemistry associated with amino acid racemization, which could eventually lead to a more accurate application of D/L amino acid measurements in age determination studies.

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